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UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF ALABAMA
SOUTHERN DIVISION

IN RE: CHANTIX (VARENICLINE) PRODUCTS LIABILITY LITIGATION	Master File No. 2:09-CV-2039-IPJ MDL No. 2092
This Document Relates To: ALL CASES	

DEFENDANT PFIZER INC'S INTRODUCTORY STATEMENT
RELEVANT TO ALL REPLY MEMORANDA

REQUEST FOR EVIDENTIARY HEARING

Pursuant to *Daubert* and Federal Rule of Evidence 702, Defendant Pfizer Inc ("Pfizer") requests that the Court hold an evidentiary hearing at which the Court and Pfizer's counsel have the opportunity to examine Plaintiffs' experts before any of them testify in front of a jury.

PRELIMINARY STATEMENT

Reliable scientific testimony is the product of an intellectually rigorous process, one that is "conservative and does not leap to specific conclusions about causation or toxicity from incomplete evidence or broad principles." *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1248 (11th Cir. 2005). Outside the courtroom, when scientists reach conclusions, it means that they have carefully reviewed the totality of relevant science, tested their theories using reliable methods over a range of scales, calculated error rates, and taken other precautions to make sure that these conclusions are based on a reliable process. Real-world scientists do not disregard data that do not support their conclusion; they do not alter their established methods to reach a desired result; and they do not ignore fundamental scientific principles, such as replication, consistency, and dose-response. Plaintiffs' experts have eschewed these scientific principles in favor of a "conclusion-oriented" process devoid of intellectual rigor and scientific integrity.

Magistrini v. One Hour Martinizing Dry Cleaning, 180 F. Supp. 2d 584, 607 (D.N.J. 2002); *see also Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999).

Plaintiffs claim that their experts formed their causation opinions based on a "weight of the evidence" approach. But rather than weighing the data "based on methods and procedures of science," *Magistrini*, 180 F. Supp. 2d at 602-03, Plaintiffs' experts simply pick and choose what they like from the scientific landscape, focusing on data that support their opinions and dismissing all contrary evidence as unreliable. *See Lust v. Merrell Dow Pharms., Inc.*, 89 F.3d 594, 596 (9th Cir. 1996). They offer no "weighing" process that can be verified using objective criteria and generally accepted standards from the scientific community. That is not a reliable methodology under *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579 (1993).

Plaintiffs' experts' "conclusion-oriented" process is evident throughout their analysis. They rely on a small subset of clinical trial data from 2005, but dismiss as unreliable data from a larger body of Pfizer's clinical trials available today. They rely on data from uncontrolled studies, case reports, and post-marketing adverse event reports, but reject the recent results of controlled observational studies designed by FDA and European regulators to evaluate the neuropsychiatric safety of Chantix. And they rely on outdated comments from regulatory agencies based on anecdotal data, but ignore updated conclusions supported by evidence

from controlled studies. In each case, Plaintiffs' experts find the evidence reliable if it supports their opinions and reject it if it does not. *See Magistrini*, 180 F. Supp. 2d at 608.

Plaintiffs' experts also selectively ignore established causation criteria when those criteria do not support their pre-ordained conclusions. While Plaintiffs pay lip service to the importance of consistency, dose-response, and biological plausibility, their experts do not reliably address these criteria. Rather than evaluate the "totality of evidence" to determine whether a consistent association is present, Plaintiffs' experts cherry-pick favorable data and dismiss all inconsistent results. *See In re Bextra & Celebrex Mktg. Sales Practices and Prod. Liab. Litig.*, 524 F. Supp. 2d 1166, 1176 (N.D. Cal. 2007). They avoid addressing dose-response because the clinical trial data do not show that depression-related events are any more common in patients taking higher doses of Chantix, a finding that does not support a dose-response or causal relationship. *See McClain*, 401 F.3d at 1242. And they come forward with a biological plausibility theory that is based on "unsubstantiated analogies," *id*. at 1240, and that is contradicted by the current body of epidemiological data. *See Raynor v. Merrell Pharms. Inc.*, 104 F.3d 1371, 1375 (D.C. Cir. 1997).

More troubling still is Plaintiffs' experts' reliance on obsolete evidence. Science marches on, but Plaintiffs and their experts are stuck in the past, relying on

fragments of clinical trial data from 2005 or questions that were raised following high-profile adverse event reports in 2007 rather than what is known in 2012. They consistently ignore data from recently completed clinical trials and controlled observational studies – all of which show no evidence that Chantix use is associated with an increased risk of serious neuropsychiatric events – and disregard the current views of the regulatory community. Just as a judge would not base a decision on outdated law or a repealed statute, Plaintiffs' experts cannot form reliable opinions based on evidence that ignores the current "state of science as it is." *Rider v. Sandoz Pharms. Corp.*, 295 F.3d 1194, 1202 (11th Cir. 2002).

It is, thus, not surprising that Plaintiffs' experts have arrived at conclusions that are at odds with more recent determinations of the scientific community, including numerous regulatory bodies and other independent organizations. *See McClain*, 401 F.3d at 1239. In 2009, for example, the European Medicines Agency ("EMA") concluded that "the current evidence does not support a causal relationship between smoking cessation using varenicline and the occurrence of SRE [suicide-related events] or other depressive disorders." CHMP Final Assessment Report, Jan. 22, 2009, at 11 (Ex. 55). Earlier this year, an independent review of the clinical data published by the Cochrane Collaboration concluded that "[t]here is little evidence from controlled studies of any link between [Chantix] and

psychiatric adverse events." Cahill et al., COCHRANE DATABASE SYS. REVS. 2012, Issue 4 at 14 (Ex. 69).

Just two weeks ago, the Department of Defense ("DOD") released a final report from its controlled observational study of nearly 36,000 patients, which found that there was "no analytic evidence to support an increased rate of severe neuropsychiatric events in new users of varenicline as compared to new users of the NRT patch when followed up for 30 or 60 days after first prescription." Pharmacovigilance Center Rep. for FDA, May 4, 2012, at 27 (Ex. 167). The DOD study found that patients taking Chantix for smoking cessation have a significantly *lower* risk of neuropsychiatric events than patients using the nicotine patch – a smoking cessation therapy Plaintiffs acknowledge is not associated with such adverse events. And the current FDA-approved Chantix label does not state that Chantix causes, or even increases the risk of, serious neuropsychiatric events, *see* Chantix Label, Nov. 2011, at 1-2 (Ex. 140), language that would be expected in the label if FDA had concluded that causation, or even a valid association, existed based on the totality of evidence today.

To date, no regulatory agency or reputable scientific body has found reliable evidence of an increased risk, let alone of a causal relationship. To further confirm these findings, both FDA and EMA have asked Pfizer to conduct additional studies to evaluate the safety of Chantix, studies which dozens of independent

investigators and ethics review boards around the world have approved. Those regulatory agencies and independent scientists could not ethically go forward with those studies if there were any reliable evidence of a causal relationship between serious neuropsychiatric events and the use of Chantix. *See* Pfizer's Intro. & Statement of Facts Relevant to All *Daubert* Motions, at 53 (Doc. No. 582).

It is in this context that the Court must consider the admissibility of Plaintiffs' experts' testimony. Plaintiffs are asking this Court to allow their experts to offer opinions – based on unreliable methods and stale science – in federal court that no reputable scientific body is willing to offer outside the courtroom. But the federal courtroom is not the place for consideration of conjecture or unproven hypotheses. *See Allison v. McGhan Med. Corp.*, 184 F.3d 1300, 1322 (11th Cir. 1999); *Rider*, 295 F.3d at 1202. It is a place for resolution of legal disputes based on what is reliably known at the time, not what is suspected or may be known in the future. *See Allison*, 184 F.3d at 1322. As the Eleventh Circuit stated in *McClain*, the "[l]aw lags science; it does not lead it." 401 F.3d at 1247 (quoting *Rosen v. Ciba-Geigy Corp.*, 78 F.3d 316, 319 (7th Cir. 1996)).

For these reasons, and as discussed in detail in the six reply briefs that follow, the Court should exclude the causation testimony of Drs. Olmstead, Furberg, Kramer, Bechara, Glenmullen, and Boyd.

Dated: June 29, 2012

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on June 29, 2012, I electronically filed the foregoing with the Clerk of the Court using the CM/ECF system which will send notification to the attorneys of record.

s/ Andrew B. Johnson
OF COUNSEL